

REMARKS:

Claims 1-3 and 5-19 are in the case and presented for consideration.

Claims 1-3 and 5-19 have been amended to improve their form.

Claims 4 and 20-25 were previously canceled, subject to applicant's right to claim their subject matter in one or more continuing applications.

At the outset, Applicant respectfully highlights that Claim 1 has already been amended to clarify that the claimed technical solution is directed to pharmaceutical composition containing (OC-6-43)-bis(acetato)-(1-adamantylamine)-amine-dichloroplatinic platinum complex of formula (II) as an active substance in a mixture with at least one pharmaceutically acceptable excipient wherein it is formed of a granulate with particles smaller than 0.5 mm in size prepared by wet granulation of a mixture of platinum complex of tetravalent platinum of formula (II) wetted by water, at least one neutral saccharide and at least one native and/or modified polysaccharide. See Amendment and Response dated April 27, 2009. Support for that amendment may be found at least at paragraphs [0020], [0021], [0028], [0039], [0040] and [0041] of the published application.

Rejections Under 35 U.S.C. §103(a)

Claims 1-11 have been rejected under 35 U.S.C. §103(a) as being unpatentable over the publication by Mckeage et al. in *Cancer Chemot. Pharmacol* (1995) ("Mckeage et al.") in view of U.S. Patent No. 6,503,943 Zak et al. ("Zak et al."), and U.S. Patent No. 6,221,393 to Collaueri et al. ("Collaueri et al."), and further in view of U.S. Patent No. 5,256,653 to Keppler et al. ("Keppler et al.") and U.S. Patent No. 5,900,252 to Calanchi et al. ("Calanchi et al.") as evidence by Swarbrick-Encyclopedia (1998). Official Action at p. 2.

The Office asserts that the claims are not directed to solving a technical solution but merely to a pharmaceutical composition containing platinum complex in a mixture of at least one pharmaceutical acceptable excipient formed of a granulate with particles smaller than 0.5 mm in size. Accordingly, the Office holds, in view of the combination of references, that it would have been *prima facie* obvious for one of ordinary skill in the art to have used the teachings of the prior art to obtain the claimed invention with a reasonable expectation of success. *Id.* at p. 3

The Office disagrees with the view that Zak does not contribute to anticipation of claim 1. It is asserted that Zak was introduced to show that inclusion of excipients to form a platinum complex was known in the prior art before filing of the present application, and that Zak ties in with the teachings of Mckeage et al. Zak was also employed for its teaching that the platinum complex is (OC-6-43) Bis (acetato)-(1-adamantylamine)-amine-dichloroplatinum. Thus compounds of claims 1 and 4 were held to be obvious variations of formula (I), wherein the complex comprises a native saccharide, cyclodextrin, that may also be modified. *Id.* at p. 4

The Office further asserts that the combined teachings of the references would have suggested to those of ordinary skill in the art to formulate a pharmaceutical composition containing a platinum complex. Using the specification to interpret the meaning of the claims, the Office asserts that McKeage et al. teach the formulation in Example I of the specification wherein the composition for wet granulation comprises a platinum IV complex (i.e., JM 216), a modified starch (i.e., sodium starch glycolate); microcrystalline cellulose (i.e., a polysaccharide) and lactose. *Id.*

The Office acknowledges that Mckeage et al. lacks the teaching that the formulation is produced by wet granulation with particles smaller than 0.5 mm. It is asserted, however,

that Kaplan et al. teach wet granulation of platinum IV complexes in a 0.5 mm range of particle size. *Id.* at pp. 4, 5.

The Office considers irrelevant with respect to the rejection under 35 U.S.C. §103 the argument that Collaueri does not teach a platinum complex, because Collaueri is used to show that granules entering into pharmaceutical compositions are advantageously prepared from a polysaccharide having particles less than 100 μ M, which is less than 0.5 mm, and therefore is alternatively relevant to the formulation itself. *Id.* at p. 5

The Office is unconvinced by the argument that different polysaccharides are used in Collaueri because the skilled artisan, it is asserted, would have been motivated to employ polysaccharides other than xanthum gums in a wet granulation process with a neutral saccharide and a polysaccharide, as claimed in claim 2, because no specific type of polysaccharide is required in claims 2 and 6. The Office also notes that Collaueri teaches that the composition is produced or processed by wet granulation. *Id.*

Thus, the Office holds that one of ordinary skill in the art would have substituted Mckeage et al.'s platinum IV complex with Zak's platinum complex to formulate a tablet by a wet granulation process because wet granulation is used to improve flow, compressibility, bio-availability, and homogeneity of low dose blends, electrostatic properties of powders, and stability of dosage forms. It is further held that one of ordinary skill in the art would have reasonably expected success in substituting Mckeage's compound JM 216 with Zak's compound ((OC-6-43) Bis(acetato)-(1-adamantylamine)-amine-dichloroplatinum) because both compounds are used for the same treatment conditions and substituting one for the other is within the purview of the skilled artisan. *Id.* at pp. 5, 6.

For the reasons that follow, Applicant respectfully traverses this rejection.

First, Applicant respectfully disagrees with the position that "the claims are not directed to solving a technical solution but merely to a pharmaceutical composition." Office Action at p. 3.

It is respectfully submitted that the finding of a combination of excipients and processing conditions providing highly desirable - yet unknown - properties of a final pharmaceutical composition should be regarded as technical solution. Further, such a technical solution is unobvious, since the mentioned combination was not obviously derivable by the skilled person in the prior art.

In Applicant's view, the critical issue, rather, is whether the technical solution of the combination of the excipients and the processing conditions as found in the framework of the presently-claimed invention is obvious in view of the cited references.

The technical problem solved by the Applicant was to eliminate the problem arising during the preparation of the pharmaceutical composition containing, as active ingredients, (OC-6-43)-bis(acetato)-(1-adamantylamine)-amine-dichloroplatinic platinum complex of formula (II) (hereinafter "compound (II)") which problem was brought about by some undesirable physical properties of compound (II) (e.g., almost insoluble in water, small bulk density, small tap density, high electrostatic charge) (see paragraph [003] of the published application).

In trying to solve this problem, an artisan of ordinary skill may have considered wet granulation. But, the wet granulation carried out with the compound (II) and any excipient(s) would not have been realized with any reasonable expectation of success since it was known that the compound (II), like the other platinum IV complexes, is chemically unstable when in contact with metals or many commonly used pharmaceutical excipients. These are the very conditions to which the active ingredients are subjected

during wet granulation when the wet granulation is implemented in the customary way.

The person of ordinary skill would not have been motivated by the prior art or the cited references to carry out wet granulation with compound (II) for the following reasons:

McKeage et al. may have mentioned similar excipients to those used for the wet granulation according the presently-claimed invention, but not in any connection with wet granulation.

A person skilled in the art would not have anticipated or even estimated the behavior of the composition containing these excipients during the wet granulation of compound (II) and thus would not have any reasonable expectation of success.

With regard to Collaueri, this reference teaches a wet granulation of excipients without the active ingredient, which creates the impression that the active ingredient is thus protected against severe wet granulation conditions.

Collaueri, in fact, teaches *away* from the common granulation of compound (II) with excipients in which common granulation is proposed. At variance with such a technical prejudice, the solution according the present invention was uncovered despite the knowledge that compound (II) is known to be chemically unstable under conditions existing during the wet granulation. This should *support* the non-obviousness of the invention solution, even in view of the teachings of Collaueri.

With respect to the newly-submitted reference, Kaplan et. al., this reference concerns a platinum II complex - cisplatin - rather than platinum IV complexes, and does not describe any wet granulation with the specific excipients as called for by the solution according to the presently-claimed invention. Kaplan et al. would not have been useful or motivating at all for a person of ordinary skill in the art in reaching the knowledge that wet granulation of the platinum IV complexes could be successfully performed by using

specifically selected excipients.

In view of the foregoing, the Applicant respectfully submits that the presently-claimed invention is not obvious in view of the combination of the cited references.

In addition, none of the above-mentioned references provide a teaching which would motivate one of ordinary skill to arrive at the presently-claimed invention.

Conclusion

Accordingly, Applicants believe that all the claims are now in condition for allowance and favorable action is respectfully requested. Should there be any issues that have not been addressed to the Examiner's satisfaction, Applicants invite the Examiner to contact the undersigned attorney.

If any fees other than those submitted herewith are due in connection with this response, please charge such fees to Deposit Account No. 14-1431.

Respectfully submitted,

/NADER A. ABADIR/

Nader A. Abadir

Reg. No. 52,537

Attorney for Applicants

ph. (845) 359-7700

Dated: November 16, 2009

NOTARO & MICHALOS P.C.

100 Dutch Hill Road, Suite 110

Orangeburg, New York 10962-2100

Customer No. 21706

R:\PATAMD\J187-028\Response to 2009-07-17OA\J187-028US-AMD2.wpd